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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,287	04/13/2001	David R. Kaplan	071957-1102	4744

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EXAMINER

GABEL, GAILENE

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 09/29/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/835,287

Applicant(s)

KAPLAN, DAVID R.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 and 37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amendment Entry

1. Applicant's response, filed 6/6/03, in Paper No. 13 is acknowledged and has been entered. Claims 2, 7, and 10 have been amended. Currently, claims 1-20 and 37 are pending and are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112

2. In light of Applicant's amendment, the rejection of claims 2, 7, and 10 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-13, 15-19, and 37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Karkmann et al. (Journal of Immunological Methods, 1999) in view of McKinley et al. (Laboratory Investigation, (1991 Dec) 65 (6) 622-30 (Abstract)) or Merz et al. (Laboratory Investigation, (1995 Jul) 73 (1) 149-56 (Abstract)) for reasons of record.

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4. Claims 1-20 and 37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lollini et al. (Immunological Blackboard, 1998) in view of McKinley et al. (Laboratory Investigation, (1991 Dec) 65 (6) 622-30 (Abstract)) or Merz et al. (Laboratory Investigation, (1995 Jul) 73 (1) 149-56 (Abstract)) for reasons of record.

Response to Arguments

5. Applicant's arguments filed 6/6/03 have been fully considered but they are not persuasive.

Applicant contends that there is no motivation or reasonable expectation of success to combine McKinley or Mertz with Karkmann and Lollini because McKinley is directed to immunohistochemical staining on glass slides and Mertz is directed to staining for electron microscopy; thus, are both unrelated to flow cytometry.

Further, Applicant also argues that the claimed invention recites contacting a chaotropic agent to cells after deposition of tyramide, i.e. staining material whereas McKinley teaches use of chaotropic agent prior to staining and Mertz does not refer to chaotropic agent for any purpose; thus, both secondary references do not suggest the claimed invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does

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not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Further, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Karkmann et al. teach a method of detecting intracellular analyte in cells by flow cytometry using intracellular tyramine-based signal amplification staining technique wherein cells are washed twice with saponin buffer to remove unbound binding partners and block peroxidase activity; thus, reducing nonspecific background staining or contamination staining. Lollini et al. also teach a method and kit for detecting intracellular analyte wherein flow cytometric detection is performed after tyramide signal amplification staining technique wherein the cells are washed with a medium containing PBS, BSA and TWEEN 20, to remove unbound binding partners from the suspension. McKinley et al. is incorporated thereto, for the teaching of using chaotropic agent (guanidine thiocyanate) to wash cells before adding a detectable labeled antibody, i.e. staining, because intracellular immunoreactivity is enhanced by denaturation with guanidine isothiocyanate. Merz et al. is also incorporated thereto for the teaching of contacting cells or tissue with a chaotropic substance to improve immunostaining. Contrary to Applicant's argument, Merz et al. disclose that the combination of chaotropic substance

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pretreatment step with the biotinylated tyramine enhancement step results in a 100 to 10,000-fold boost in sensitivity without loss of specificity in staining. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute chaotropic agent as taught by McKinley or Merz to wash the cells in the flow cytometric method taught by Karkmann and Lollini because McKinley specifically taught that denaturation with guanidine isothiocyanate enhances immunoreactivity of intracellular antigens; thus enhancing sensitivity in signal amplification detection methods, and Merz specifically further confirmed that addition of chaotropic substance to cells prior to biotinylated tyramine enhancement step results to improved immunostaining to as much as 100 to 10,000-fold boost in sensitivity without loss of specificity in detecting intracellular antigens. Additionally, the "comprising" language in the claims do not exclude pretreating the cells with chaotropic agent.

6. For reasons aforementioned, no claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
September 25, 2003




CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800-1641